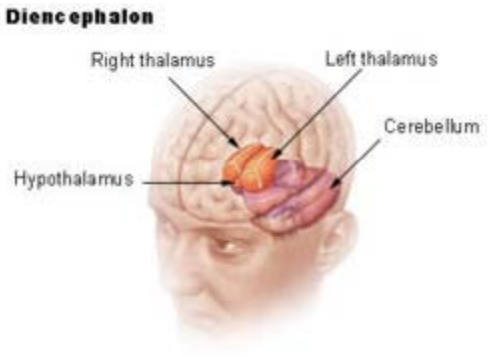
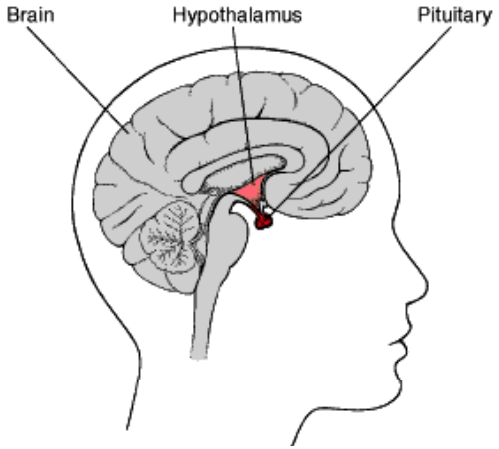
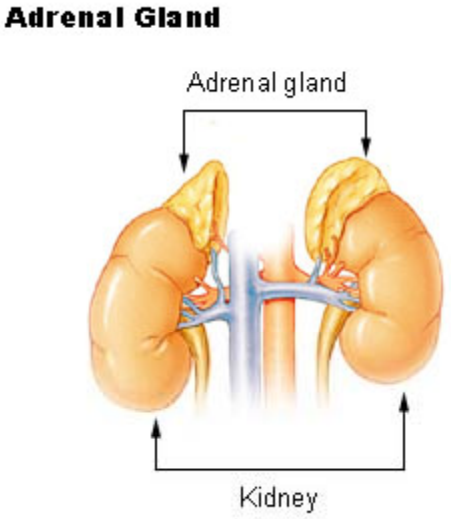
Hypothalmic-pituitary-adrenal is a complex set of direct influences and feedback interactions among the hypothalamus, the pituitary gland (a pea-shaped structure located below the hypothalamus), and the adrenal glands (small, conical organs on top of the kidneys).The interactions among these organs constitute the HPA axis, a major part of the neuroendocrine system that controls reactions to stress and regulates many body processes.







Early life events (experience)
Variation in maternal care of rats

Affect brain development, stress reactivity of offspring

exposure to stress hormones

Vulnerability for stress-induced illness

Mental disorders; social life

Affect the next generation?

How does maternal behavior transmit to the next generation?

Nongenomic Transmission Across Generations of Maternal Behavior and Stress Responses in the Rat

Darlene Francis, Josie Diorio, Dong Liu, Michael J. Meaney*

In the rat, variations in maternal care appear to influence the development of behavioral and endocrine responses to stress in the offspring. The results of cross-fostering studies reported here provide evidence for (i) a causal relationship between maternal behavior and stress reactivity in the offspring and (ii) the transmission of such individual differences in maternal behavior from one generation of females to the next. Moreover, an environmental manipulation imposed during early development that alters maternal behavior can then affect the pattern of transmission in subsequent generations. Taken together, these findings indicate that variations in maternal care can serve as the basis for a nongenomic behavioral transmission of individual differences in stress reactivity across generations.

How does individual personality (individual differences in behavioral traits) transmit through generations?

1. Genomically transmitted mechanism
   (gene-coded behavioral traits)

2. Nongenomically transmitted mechanism?
   (not through genetic, but through behavior)?

Norway rat,

Natural variations in maternal care affect:

→Offspring differences in behavioral response to stress
→Offspring differences in endocrine response to stress

Norway rat,

Offspring of high LG mothers

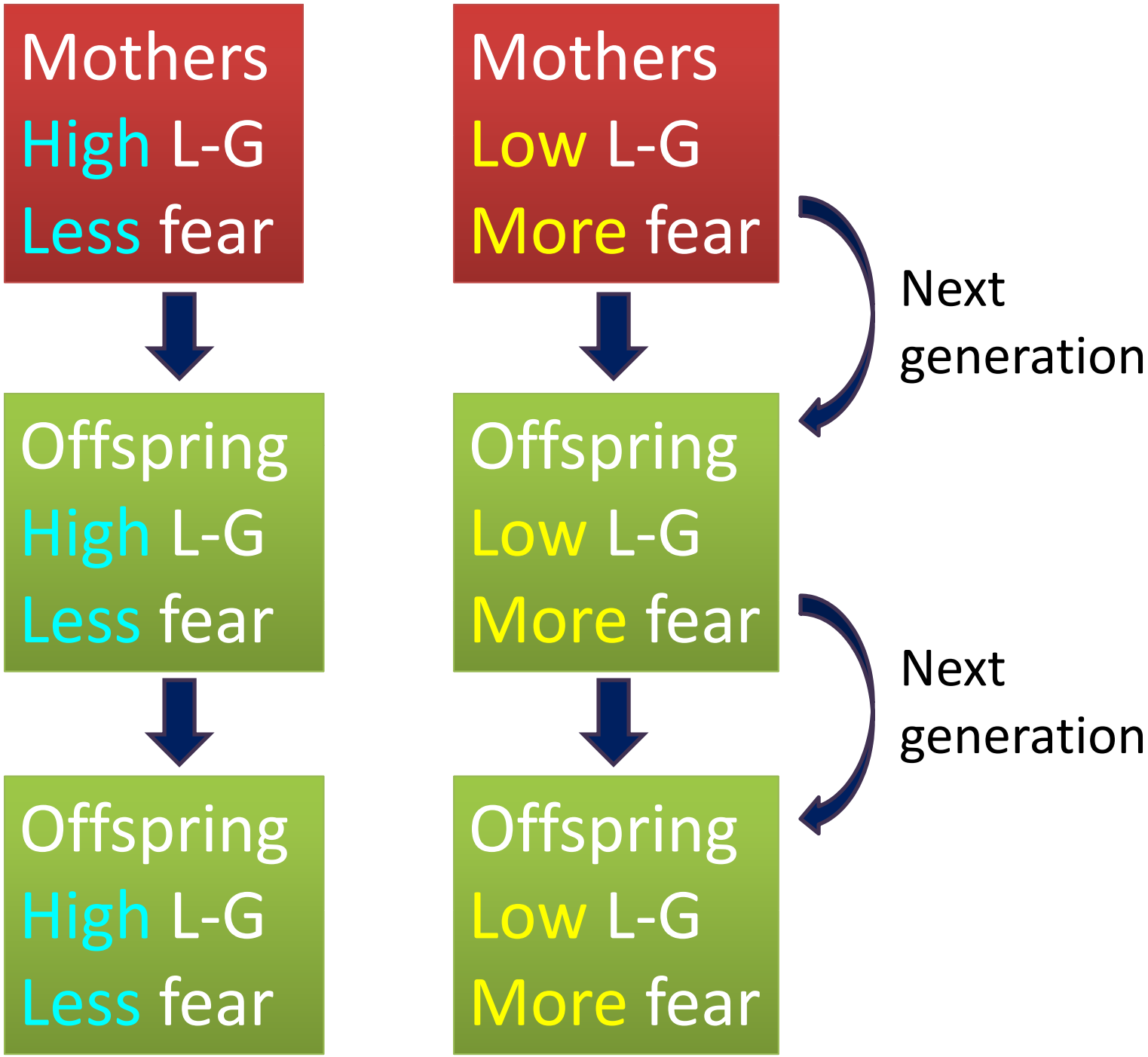
→ less fearful, more HPA response to stress

→ when grow up, high LG to their pups

Offspring of low LG mothers

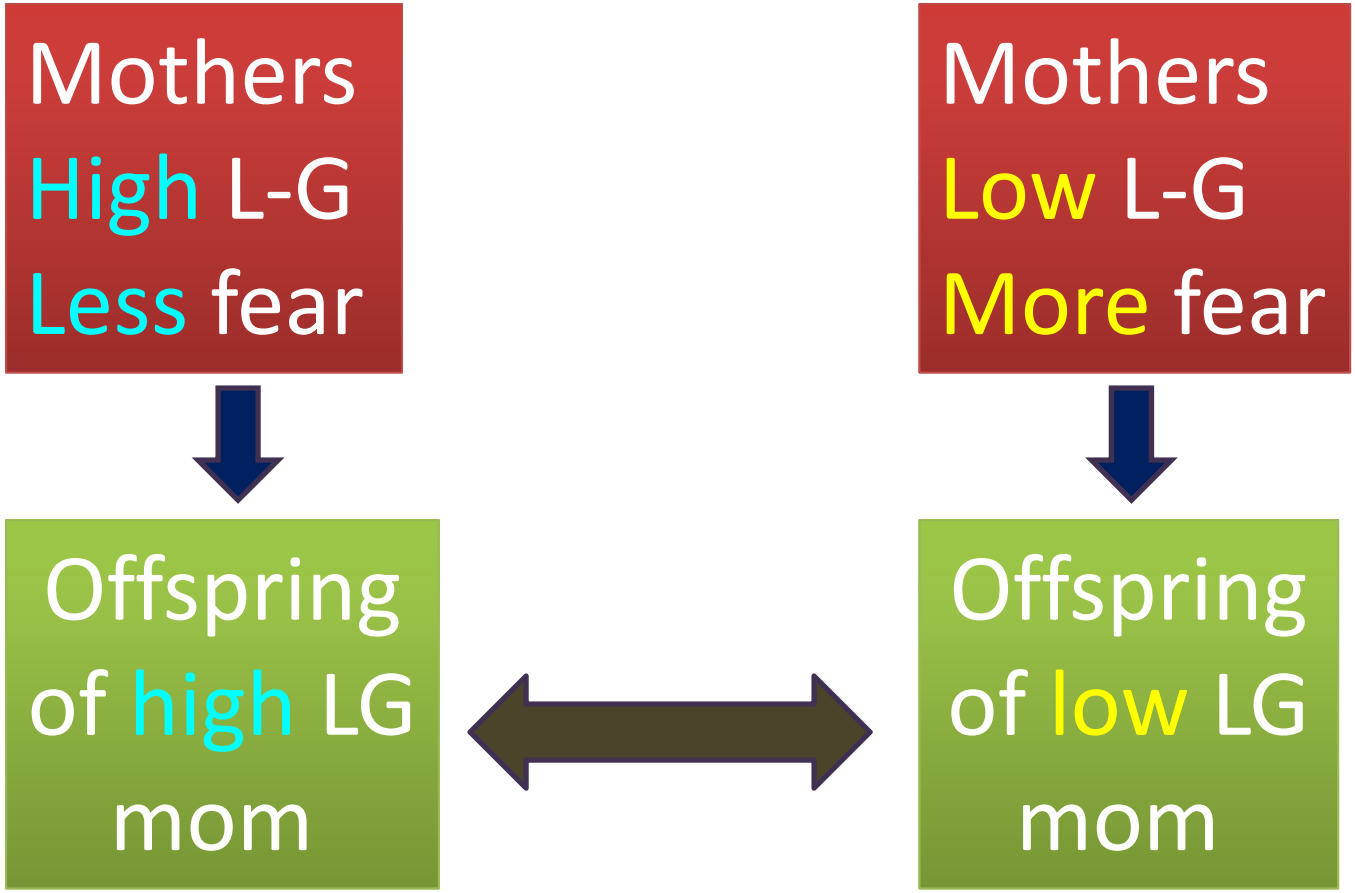
→ more fearful, less HPA response to stress

→ when grow up, low LG to their pups

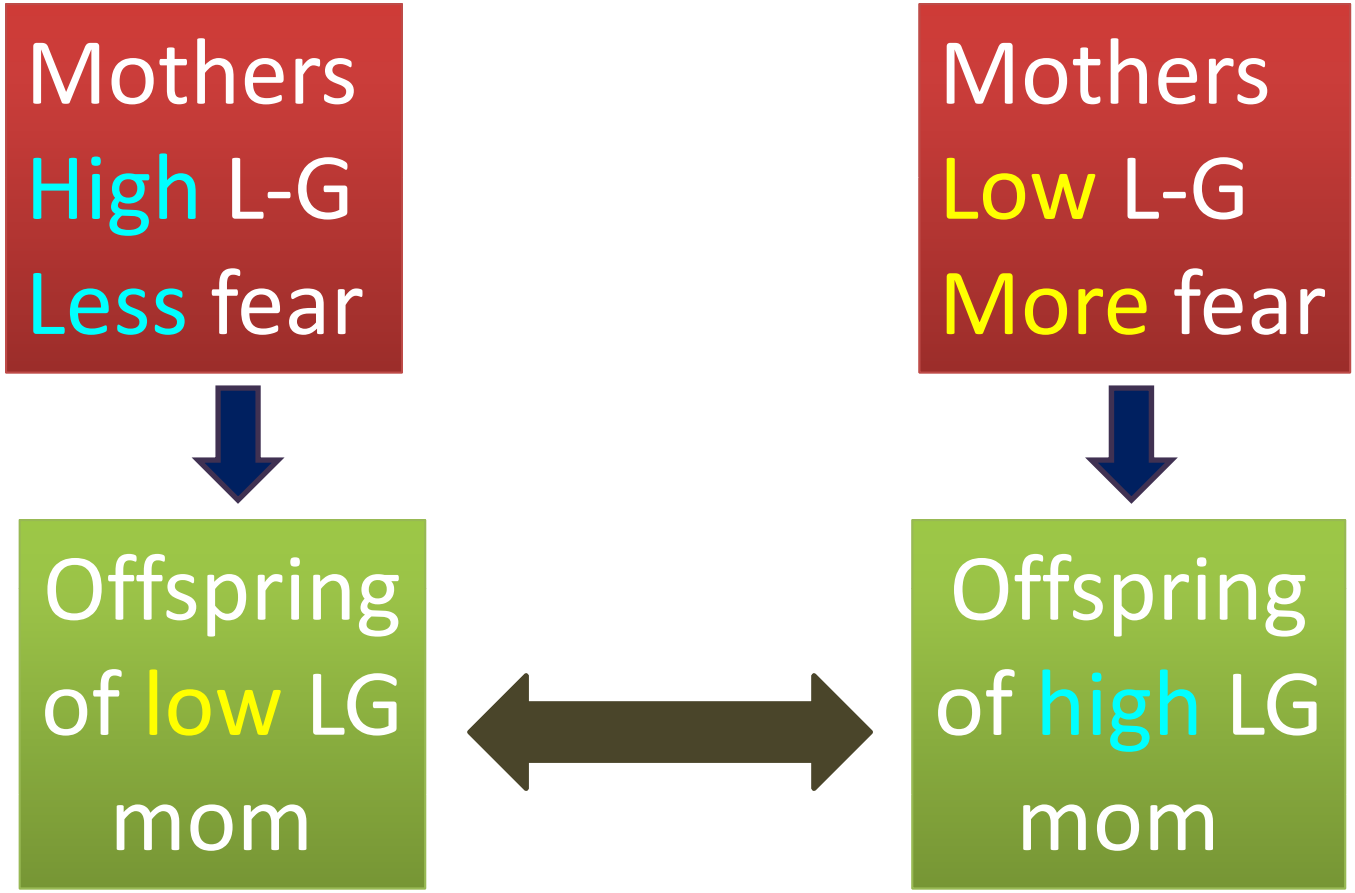

Mothers
High L-G
Less fear
Mothers
Low L-G
More fear
Next generation
Offspring
High L-G
Less fear
Offspring
Low L-G
More fear
Next generation
Offspring
High L-G
Less fear
Offspring
Low L-G
More fear

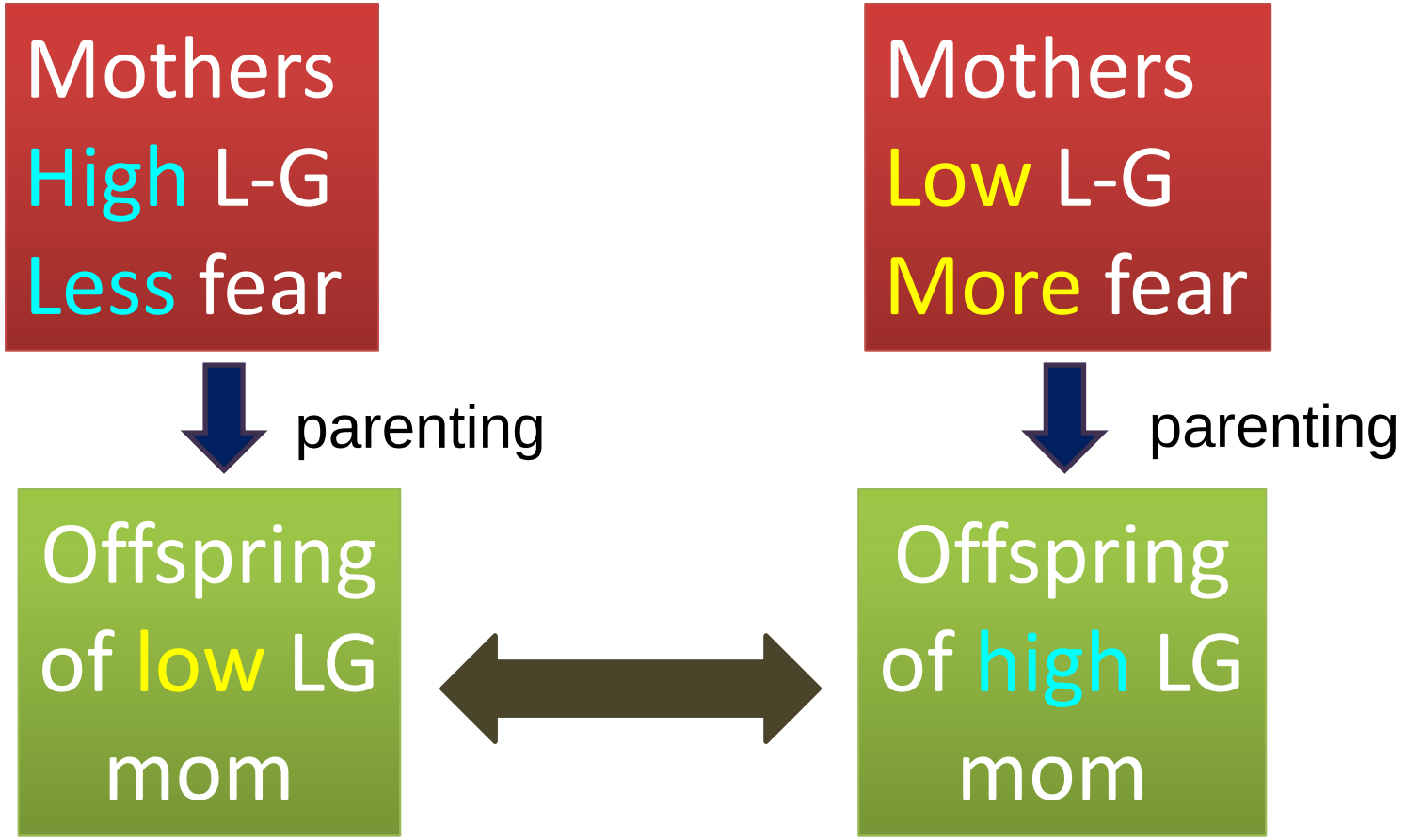
How do we determine if maternal care behavior is genetically or non-genetically transmitted?

Cross-fostering experiment !!!



Switch the pups!

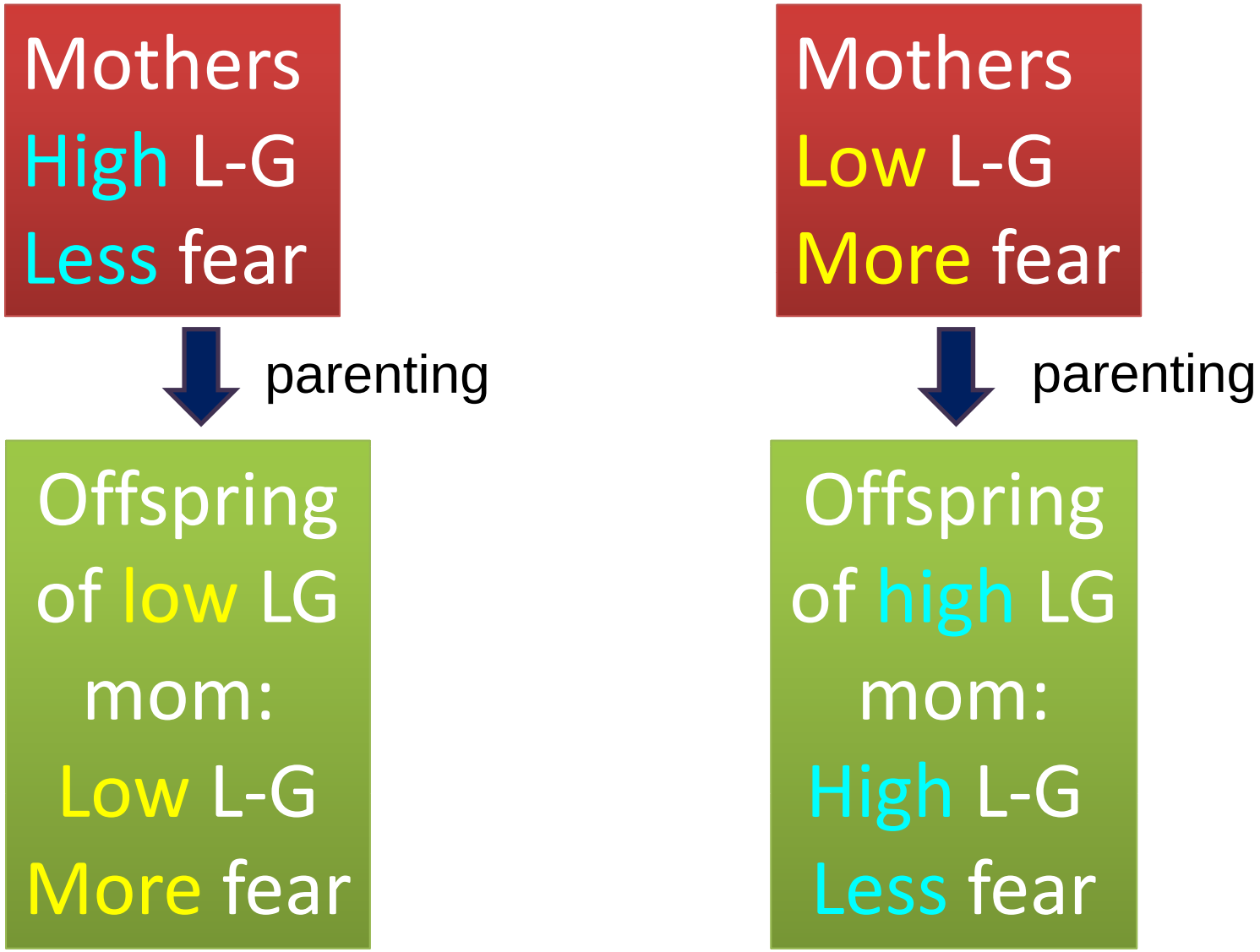

Mothers
High L-G
Less fear
Mothers
Low L-G
More fear
Offspring
of low LG
mom
Offspring
of high LG
mom



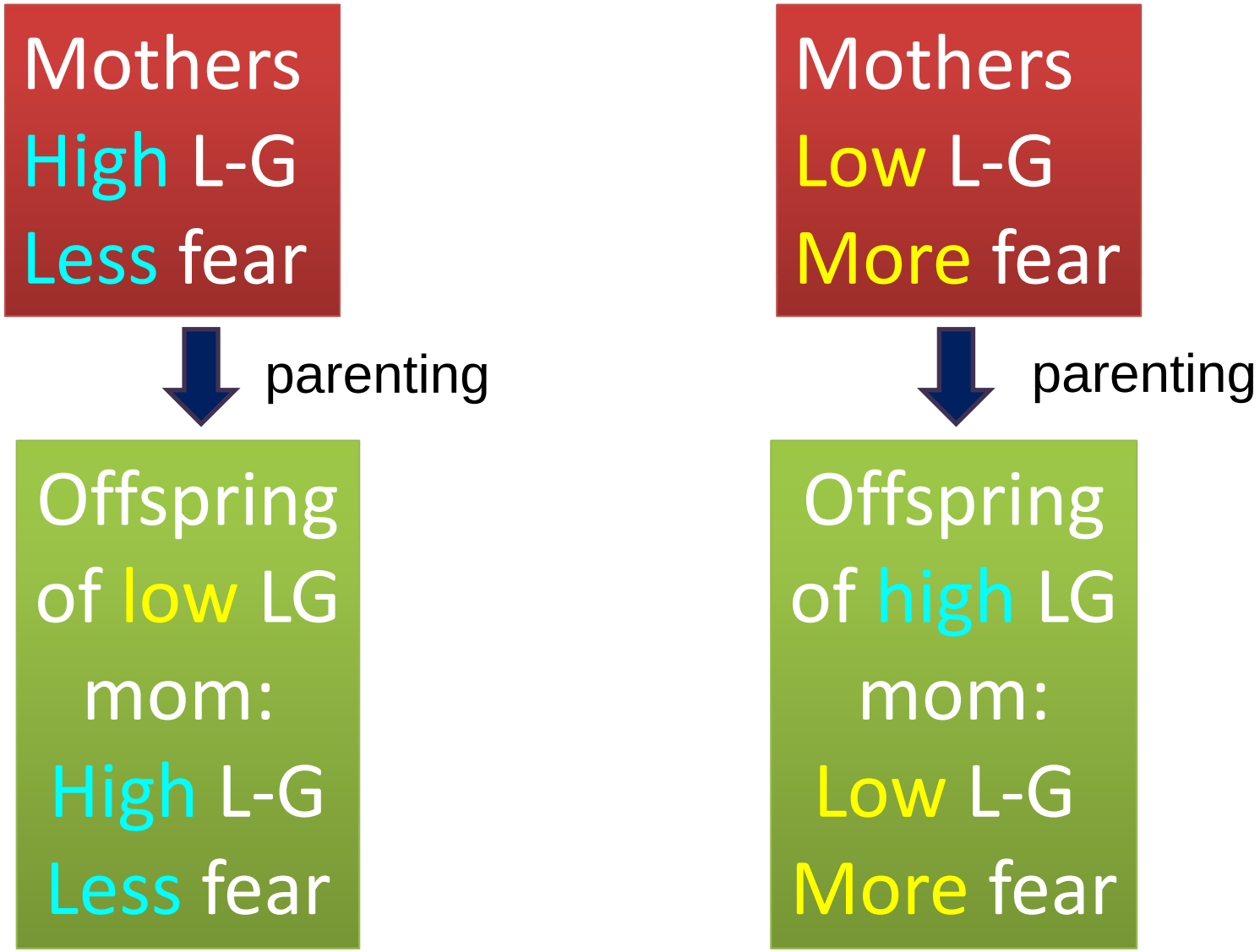
After switching the pups, will the switched offspring be

more/less fearful to stress?
have higher/lower LG when they grow up as moms?

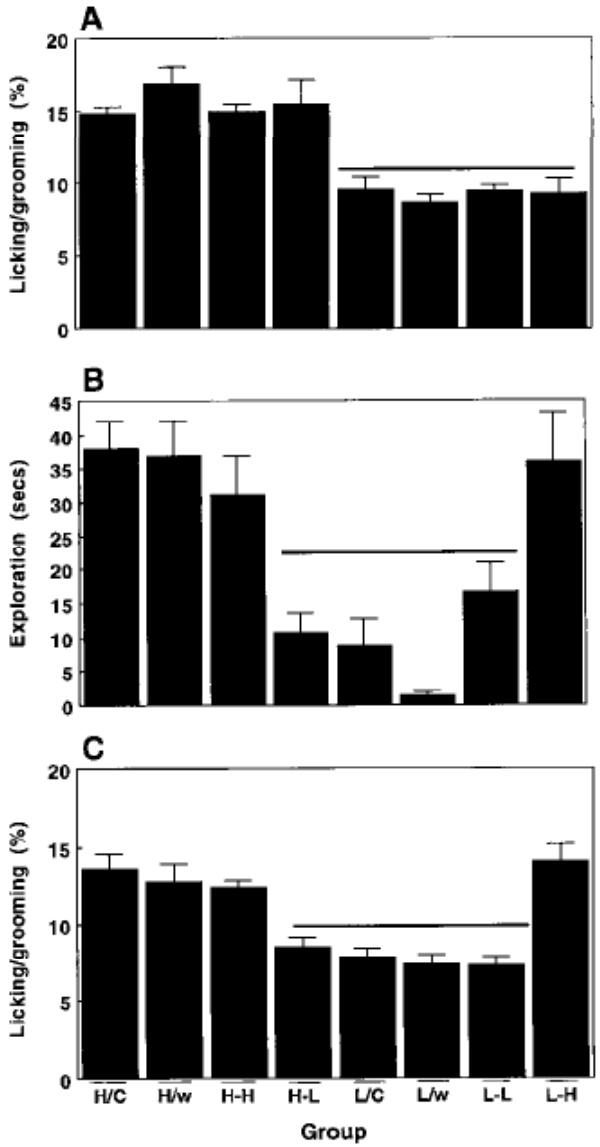
Prediction 1: if behavior is genetically transmitted, offspring-switching would not affect offspring behavior.



Prediction 2: if it is NON-genetically transmitted, offspring-switching would affect offspring's behavior.



Results: Maternal care behavior transmits to the next generation through non-genomic mechanisms.



Nongenomic transmission

Early life events (experience)
Variation in maternal care behavior

Modify epigenetic mechanism and induce molecular changes in neurons (e.g., histone modification…)

Affect brain development, stress response of offspring

Vulnerability for stress-induced illness

Mental disorders; social life

Transmit to the next generation

Nat Neurosci. 2009 March ; 12(3): 342–348. doi:10.1038/nn.2270.

Epigenetic regulation of the glucocorticoid receptor in human brain associates with childhood abuse

Abstract

Maternal care influences hypothalamic-pituitary-adrenal (HPA) function in the rat through epigenetic programming of glucocorticoid receptor expression. In humans, childhood abuse alters HPA stress responses and increases the risk of suicide. We examined epigenetic differences in a neuron-specific glucocorticoid receptor (*NR3C1*) promoter between postmortem hippocampus obtained from suicide victims with a history of childhood abuse and those from either suicide victims with no childhood abuse or controls. We found decreased levels of glucocorticoid receptor mRNA, as well as mRNA transcripts bearing the glucocorticoid receptor 1_F splice variant and increased cytosine methylation of an *NR3C1* promoter. Patch-methylated *NR3C1* promoter constructs that mimicked the methylation state in samples from abused suicide victims showed decreased NGFI-A transcription factor binding and NGFI-A–inducible gene transcription. These findings translate previous results from rat to humans and suggest a common effect of parental care on the epigenetic regulation of hippocampal glucocorticoid receptor expression.

Repeated periods of maternal separation in early life increase central noradrenaline and serotonin responses to stress in the rhesus monkey depression, early life events might predispose an individual to depression, fearful social life, difficulty with novelty in later life

Hug your baby!

Take home message:

Individual differences in behavior
and gene expression can be transmitted
from one generation to the next
through behavior (induces epigenetic reprogramming), does not require genetics.

Our differences in personality can be explained by a similar mechanism?

Evolution of social behavior

How some species are more social than others?

(proximate causes)

Why some species are more social than others?
(Ultimate causes)

More social means more adaptive?

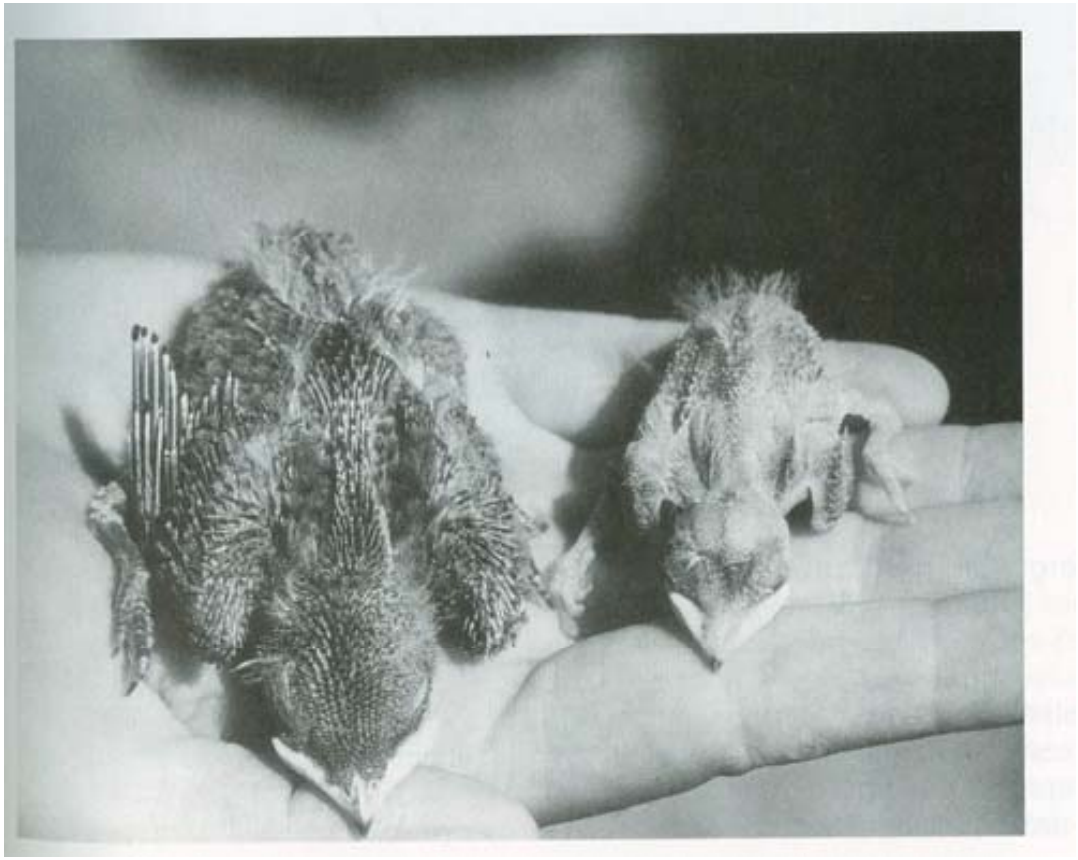
Natural selection assumes that behaviors evolve to best adaptive to species-specific ecological environment.

The benefit and cost of social life

Cost: compete for resources; parasites/diseases

Benefit: foraging, anti-predator, helper

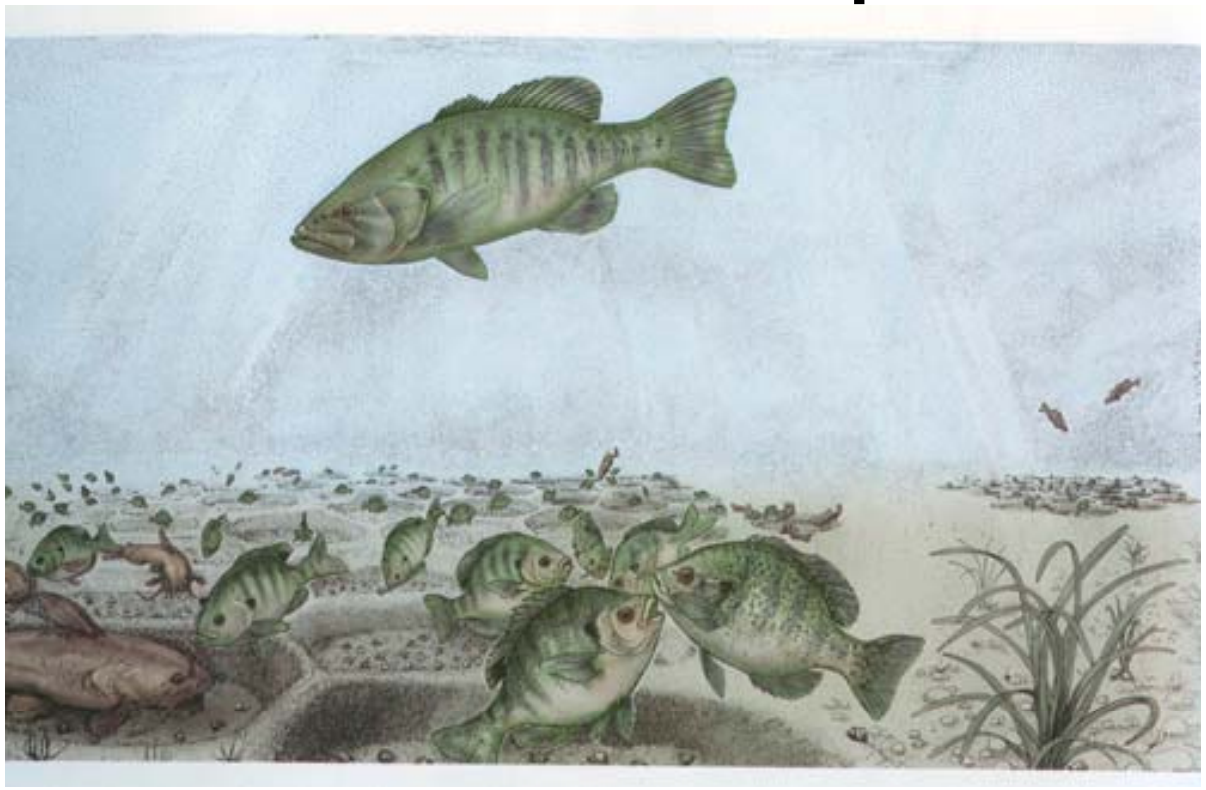
Effect of parasites on cliff swallow nestlings



Which nestling suffers from parasite infection?

Parasites (fly larvae) in cowbird nestlings

Benefit of living in a group: Mutual defense of predator



Bluegills

Helpful behavior

How does it evolve?

Until mid-1960s, biologists took helpful behavior for granted because they assumed that animals should assist one another for the benefit of the species as a whole.

Group selection or

Individual selection ?

But, does group selection work?

Lemmings (rodents)

Extreme population fluctuation

High population density →

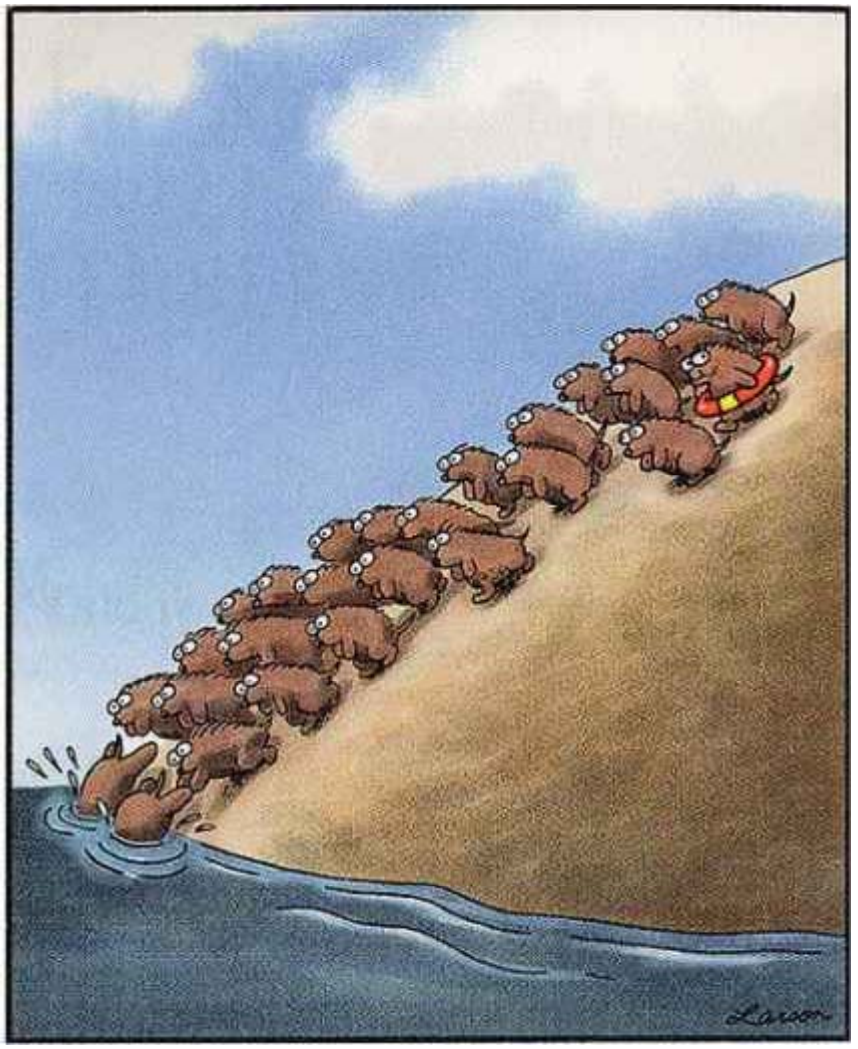
→ migration → many died

→commit suicide to control population size, for the benefit of lemming species?

Cheaters will have reproductive success, And their “cheating” genes will prevail!

Lemmings (rodents)

Group selection doesn’t work!



Types of social interactions

1. Mutualism (cooperation)
2. Reciprocity
3. Altruism
4. Selfish behavior

1. Mutualism

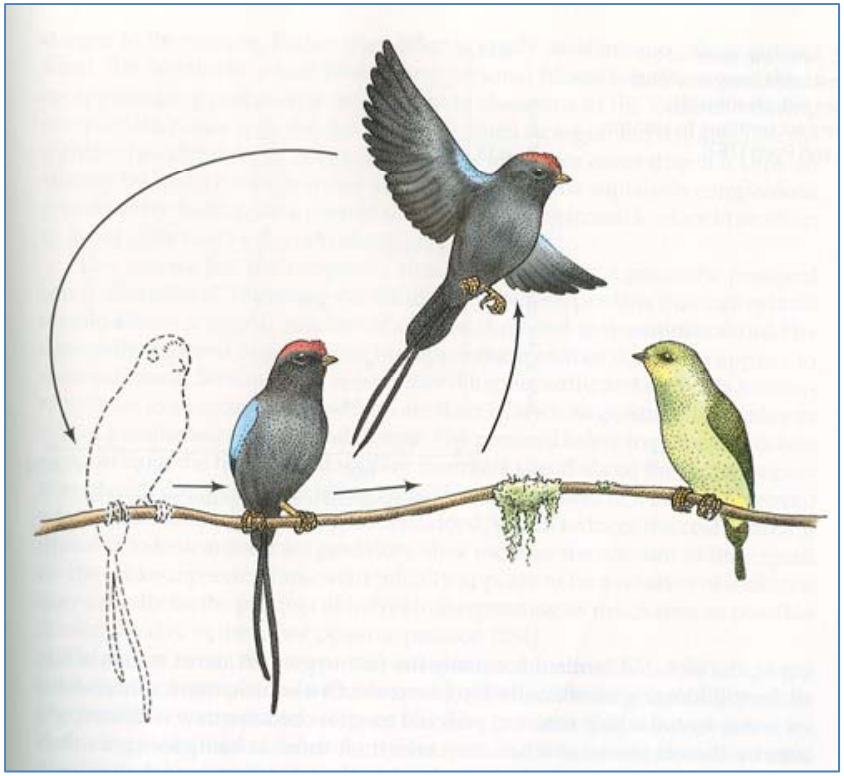
Both helper and recipient have reproductive gains from their interaction.

Cooperative courtship of the long-tailed manakin

Cooperative courtship of the long-tailed manakin

One is dominant, the other is subordinate.

Why does the subordinate help?



2. Reciprocity

Social grooming

Types of social interactions

1. Mutualism (cooperation)
2. Reciprocity
3. Altruism
4. Selfish behavior

2. Reciprocity

Both helper and recipient have reproductive gains from their interaction, but helper’s gain will be delayed.

2. Reciprocity-prisoner's dilemma

		Player B	
		Cooperate	Defect
Player A	Cooperate	Reward for mutual cooperation	Maximum punishment
	Defect	Maximum reward	Punishment for Mutual defection

Prisoner's dilemma

Payoffs for player's response ranks….

1. Defect while other player cooperate

2. Both cooperate

3. Both defect

4. Cooperate while other player defects

Optimal response: always defect, never cooperate

Reciprocity should never evolve?

If two players interact repeatedly.

“ tit for tat” strategy
(reciprocity strategy based on prisoner’s dilemma)

Tit for tat strategy

An individual cooperates on the initial encounter with a partner subsequently copies its partner's pervious move.

1. If the partner cooperates, then cooperate.
2. If the partner defects, then defects

Tit for tat strategy

Three fundamental characteristics

(1) nice: never cheats first

(2) Retaliatory: always responds to a partner that is cheating by cheating itself.

(3) Forgiving: only remembers one move back in time.

Tit for tat strategy in animals

Food sharing in blood-sucking vampire bats

Female bats regurgitate blood meals to others that failed to obtain food

Food sharing "tit for tat" in blood-sucking vampire bats

1. Bats that can recognize one another
   are more likely to give blood to those that
   have donated blood to them in the past (reciprocate)

2. Blood sharing is a huge benefit for recipient
   but not a big cost for donor.

Decision making and “tit for tat” in humans

		Player B: Cooperate	Player B: Defect
Player A	Cooperate	Reward for mutual cooperation	Maximum punishment
	Defect	Maximum reward	Punishment for Mutual defection

Playing “Tit for tat” in the fMRI (monitoring brain activity)

1.Most emotionally rewarding payoff is “both cooperate” (induce highest neural activity in brain’s reward areas);

even though the most monetary reward is to “cheat”

2. Subjects derived pleasure from punishing cheaters (induce high neural activity in reward area when punish the cheater).

3. When subjects mutually trust, oxytocin increases.

3. Altruism

Donor (helper) really does permanently lose opportunities to reproduce
as a result of helping another produce more surviving offspring.

--reduce individual’s reproductive success

How can altruism ever evolve?

1. Group selection?

2. Indirect selection (Hamilton ‘s theory)

Halmilton's kinship theory

Inclusive fitness: an individual's total fitness is based on the number of its own offspring and the contribution it makes to the reproductive success of its genetic relatives.

include both direct fitness (your own offspring) and indirect fitness (your sib's offspring, your grandchildren).

Two siblings are related to one another by **r=0.5**

Sibling #1 has gene X, 50% (0-100%) chance she received gene X from her mom.

Sibling #2 has gene X, 50% (0-100%) chance she received gene X from her mom.

There is 25% chance (50%x50%) that the siblings share gene X through their mother.

There is 25% chance that the siblings share gene X through their father.

The chance that the siblings share gene X through either their mother or father: 25% + 25% =50%

The chance that the siblings share gene X through the parents =50% r=0.5

Quiz :

The genetic related between cousins: r=0.125

The genetic relatedness between grandparents and grandchild: r=0.25